


the above named sequences, SEQ I NOS:1-41, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disc.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

The sequence identified in the instant application as SEQ ID NO:1 was inadvertently omitted from the application but was incorporated by reference to priority application 60/150,452, filed August 24, 1999. Thus, Applicants believe that entry of the sequence into the instant application does not constitute new matter.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,


Andrew T. Serafini, Ph.D.
Reg. No. 41,303

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
ATS:adm
PA 3180739 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning on page 7, line 7, has been amended as follows:

Some human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO:[38]37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

The paragraph beginning on page 7, line 13, has been amended as follows:

Other human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:[39]38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively.

The paragraph beginning on page 8, line 3, has been amended as follows:

The invention provides a hybridoma cell line comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human sequence heavy chain transgene and a human sequence light chain transgene, wherein the hybridoma produces a human sequence antibody that specifically binds to human CTLA-4. In a related embodiment, the hybridoma secretes a human sequence antibody that specifically binds human CTLA-4 or binding fragment thereof, wherein the antibody is selected from the group consisting of: a human sequence antibody comprising heavy chain heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH

(SEQ ID NO:27), FISYDGNKYYADSVKG (SEQ ID NO:32) and TGWLGPFDY (SEQ ID NO:37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVGSSYLA (SEQ ID NO:24), GAFSRAT (SEQ ID NO:29), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:17 and SEQ ID NO:7, respectively; a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO:[38]37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:19 and SEQ ID NO:9, respectively; or a human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:[39]38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:23 and SEQ ID NO:13, respectively.

Table 3, on page 74, lines 1-4, has been amended as follows:

| Chain | HuMab | CDR1 | SEQ ID NO: | CDR2 | SEQ ID NO: | CDR3 | SEQ ID NO: |
|-------------|-------|--------------|------------|-------------------|------------|------------|------------|
| Light Chain | 10D1 | RASQSVGSSYLA | 24 | GAFSRAT | 29 | QQYGSSPWT | 35 |
| | 4B6 | RASQSVSSSFLA | 25 | GASSRAT | 30 | QQYGSSPWT | 35 |
| | 1E2 | RASQGISSWLA | 26 | AASSLQS | 31 | QQYNSYPPT | 36 |
| Heavy Chain | 10D1 | SYTMH | 27 | FISYDGNKYYADSVKG | 32 | TGWLGPFDY | 37 |
| | 4B6 | SYTMH | 27 | FISYDGSNKHYADSVKG | 33 | TGWLGPFDY | [38]37 |
| | 1E2 | SYGMH | 28 | VIWYDGSNKYYADSVKG | 34 | APNYIGAFDV | [38]38 |

The paragraph beginning on page 76, line 16, has been amended as follows:

The kappa light chain plasmid, pCK7-96 (SEQ ID NO:[40]39), includes the kappa constant region and polyadenylation site, such that kappa sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and BbsI, and cloned into pCK7-96 digested with HindIII and BbsI to reconstruct a complete light chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/NotI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

The paragraph beginning on page 76, line 23, has been amended as follows:

The gamma1 heavy chain plasmid, pCG7-96 (SEQ ID NO:[41]40), includes the human gamma1 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pCG7-96 digested with HindIII and AgeI to reconstruct a complete gamma1 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/SalI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

The paragraph beginning on page 76, line 31, has been amended as follows:

The gamma4 heavy chain plasmid, pG4HE (SEQ ID NO:[42]41), includes the human gamma4 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pG4HE digested with HindIII and AgeI to reconstruct a complete gamma4 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/EcoRI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.